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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/660,798	09/12/2003	H. Paul Redmond	1194-282	6154

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EXAMINER

ANDERSON, JAMES D

ART UNIT	PAPER NUMBER
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1614

DATE MAILED: 07/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/660,798	Applicant(s) REDMOND ET AL.	
	Examiner James D. Anderson	Art Unit 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 May 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-11 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-11 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Applicants' arguments, filed May 15, 2006, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous Office Actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Status of the Claims

Claims 1-11 are currently pending and are the subject of this Office Action.

Priority

No support is seen for using a combination of 5-FU and a methylol transfer agent to inhibit tumor growth as recited in the instant claims in parent applications 10/281,138 and 09/583,902. Thus, the earliest effective filing date for the instant claims has been determined to be November 28, 2000.

Claim Rejections - 35 USC § 112 – First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4, 6-8 and 10-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject

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matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-3, 6-7 and 10 are drawn to methods of inhibiting tumor growth with a combination of 5-fluorouracil and a "methylol transfer agent" (Claim 1, Line 3). The specification provides two examples of methylol transfer agents: taurolidine and taurultam (page 2, paragraph 10). Nowhere, however, does the specification contemplate or describe the structural features of other "methylol transfer agent[s]" other than the specifically disclosed taurolidine and taurultam.

The instant claims are broad, being drawn to the use of a "methylol transfer agent" in general, however applicants have not provided any structural features or any other means for the skilled artisan to appreciate exactly what compounds are considered to be methylol transfer agents. The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described. Univ. of Rochester v. G.D. Searle, 69 USPQ2d 1886, 1892 (CAFC 2004). Applicants have provided no means for the skilled artisan to visualize or recognize what compounds, aside from taurolidine and taurultam, are included in the phrase "methylol transfer agents."

Claims 4, 8 and 11 are drawn to methods of inhibiting tumor growth with a combination of 5-fluorouracil and taurolidine, taurultam or "a biologically active derivative thereof" (Claim 4, Line 2). Nowhere does the specification contemplate or describe the structural features of biologically active derivatives of taurolidine and

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taurultam. The skilled artisan is provided with no guidance on how to synthesize a biologically active derivative of taurolidine or taurultam or what structural features the applicants consider to be essential for a compound to be a "biologically active derivative" of taurolidine or taurultam.

The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described. Univ. of Rochester v. G.D. Searle, 69 USPQ2d 1886, 1892 (CAFC 2004). Applicants have provided no means for the skilled artisan to visualize, recognize or synthesize any "biologically active derivative[s]" of taurolidine or taurultam.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

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consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carter in view of WO 92/00743 for the reasons set forth in the Office Action mailed 12/15/2005.

Carter discloses that 5-FU is useful to treat the instantly recited cancers (see especially page 78). The reference differs from the instant claims in that it does not disclose a combination therapy comprising 5-FU and taurolidine or taurultam to treat cancer.

However, WO 92/00743 discloses a method of treating cancer with taurolidine and taurultam (pages 1-3). The reference also contemplates co-administering taurolidine and/or taurultam with "other agents known to be involved in tumor metabolism" or "cytotoxic agents" (page 3, first paragraph).

Claims 1-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carter in view of U.S. Patent No. 6,303,596 for the reasons set forth in the Office Action mailed 12/15/2005.

Carter discloses that 5-FU is useful to treat the instantly recited cancers (see especially page 78). The reference differs from the instant claims in that it does not disclose a combination therapy comprising 5-FU and taurolidine or taurultam to treat cancer.

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However, the '596 patent discloses a method of treating cancer with taurolidine and taurultam (abstract, claims).

It would have been *prima facie* obvious to combine 5-fluorouracil and taurolidine or taurultam to treat cancer. Taurolidine and 5-FU are individually known in the art as agents for treating cancers, whose efficacy when administered alone is well established for the treatment of a large number of neoplasias and metastasis. It is generally obvious to combine two compositions, each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose. *In re Kerkhoven*, 205 U.S.P.Q. 1069 (CCPA 1980). The idea for combining said compositions flows logically from their having been individually taught in the prior art. *In re Crockett*, 126 U.S.P.Q. 186, 188 (CCPA 1960).

Accordingly, to establish obviousness in such fact situations it is NOT necessary that the motivation come explicitly from the reference itself. The natural presumption that two individually known anticancer agents would, when combined, provide a third composition also useful for treating cancer flows logically from each having been individually taught in the prior art. Applicant has presented no evidence (e.g. unexpected results) to rebut this natural presumption.

Response to Arguments

As stated in the Office Action of December 15, 2005 and reiterated above, it would have been obvious to combine 5-FU and taurolidine in compositions and

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methods to treat cancer. It is generally obvious to combine two compositions, each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.

Applicant's arguments filed May 15, 2006 have been fully considered but they are not persuasive. Applicants argue that they have "described and shown an unexpected synergistic effect of the combination of 5-FU and a methylol transfer agent in the treatment of cancer" (page 8 of Applicant Response). This is not convincing as the argument is based on an allegation of unexpected results. On page 3, paragraph 18 of the instant specification, there is only a statement that taurultam and taurolidine "substantially enhance and augment the antineoplastic effects of 5-FU." However, the application does not supply any pharmacological data to corroborate this statement. Similarly, the only example provided in the specification (Example 1, page 5) simply states "Taurolidine was found to augment the effects of given doses of 5-FU." It is not clear exactly what "augment" means with regard to the effect of taurolidine on 5-FU. Both compounds are known in the art to be effective treatments for cancer as discussed *supra*. In the absence of any particular details with respect to the unexpected results applicants claim they have demonstrated, the obviousness rejections are maintained. For example, to demonstrate unexpected results commensurate in scope with the claims, applicants need to show that a combination of 5-FU and taurolidine results in greater inhibition of cell proliferation than would be expected if the effects of each agent individually were added together. An additive effect would be expected and not evidence of surprising results.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-11 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2 of U.S. Patent No. 6,479,481. Although the conflicting claims are not identical, they are not patentably distinct from each other because '481 discloses a method of treating tumors using the methylol

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transfer agents taurolidine, taurultam or a mixture thereof and that they may be combined with 5-FU to treat glioblastoma (column 9, lines 13-43).

Applicants appear to acquiesce, as the response filed May 15, 2006 did not traverse this rejection but did indicate that applicants would be willing to file a Terminal Disclaimer "should any conflicting claims be found allowable." As no such claims have been found allowable, the rejection is maintained.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James D. Anderson whose telephone number is 571-272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



James D. Anderson
Examiner
Art Unit 1614

July 7, 2006



ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER